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UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	AL01348K1B
First Inventor	Robert G. Aslanian et al.
Title	Novel Non-Imidazole Compounds
Express Mail Label No.	EV334445188 US

APPLICATION ELEMENTS

See MPEP chapter 600 concerning utility patent application contents.

ADDRESS TO: Mail Stop Patent Application, Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450

17510 U.S. PTO 10/699189 10/31/03

1. ☒ Fee Transmittal Form (e.g., PTO/SB/17) *(Submit an original and a duplicate for fee processing)*
2. ☐ Applicant claims small entity status. See 37 CFR 1.27.
3. ☒ Specification [Total Pages 152] *(preferred arrangement set forth below)*
   - Descriptive title of the invention
   - Cross Reference to Related Applications
   - Statement Regarding Fed sponsored R & D
   - Reference to sequence listing, a table, or a computer program listing appendix
   - Background of the invention
   - Brief Summary of the Invention
   - Brief Description of the Drawings *(if filed)*
   - Detailed Description
   - Claim(s)
   - Abstract of the Disclosure
4. ☐ Drawing(s) (35 U.S.C. 113) [Total Sheets]
5. Oath or Declaration [Total Sheets]
   a. ☐ Newly executed (original or copy)
   b. ☒ Copy from a prior application (37 CFR 1.63(d)) *(for continuation/divisional with Box 18 completed)*
      i. ☐ DELETION OF INVENTOR(S) Signed statement attached deleting inventor(s) name in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b).
6. ☒ Application Data Sheet. See 37 CFR 1.76
7. ☐ CD-ROM or CD-R in duplicate, large table or Computer Program *(Appendix)*
8. Nucleotide and/or Amino Acid Sequence Submission *(if applicable, all necessary)*
   a. ☐ Computer Reader Form (CRF)
   b. Specification Sequence Listing on:
      i. ☐ CD-ROM or CD-R (2 copies); or
      ii. ☐ Paper
   c. ☐ Statements verifying identity of above copies

ACCOMPANYING APPLICATION PARTS

9. ☐ Assignment Papers (cover sheet & document(s))
10. ☐ 37 CFR 3.73(b) Statement ☐ Power of Attorney *(When there is an assignee)*
11. ☐ English Translation Document *(if applicable)*
12. ☒ Information Disclosure Statement (IDS)/PTO-1449 ☐ Copies of IDS Citations
13. ☒ Preliminary Amendment
14. ☒ Return Receipt Postcard (MPEP 503) *(Should be specifically itemized)*
15. ☐ Certified Copy of Priority Document(s) *(if foreign priority is claimed)*
16. ☐ Nonpublication Request under 35 U.S.C. 122 (b)(2)(B)(i). Applicant must attach form PTO/SB/35 or its equivalent.
17. ☐ Other: .....

18. If a CONTINUING APPLICATION, check appropriate box, and supply the requisite information below and in the first sentence of the specification following the title, or in an Application Data Sheet under 37 CFR 1.76:

☐ Continuation ☒ Divisional ☐ Continuation-in-part (CIP) of prior application No.: 09/978,267, 60/240,090

Prior application information: Examiner K. Habte Art Unit: 1614

For CONTINUATION OR DIVISIONAL APPS only: The entire disclosure of the prior application, from which an oath or declaration is supplied under Box 5b, is considered a part of the disclosure of the accompanying continuation or divisional application and is hereby incorporated by reference. The incorporation can only be relied upon when a portion has been inadvertently omitted from the submitted application parts.

19. CORRESPONDENCE ADDRESS

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Signature		Date	10/31/2003

fee purpose

AMENDMENTS TO THE CLAIMS

1. (cancelled)

2. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein R^1 is selected from:

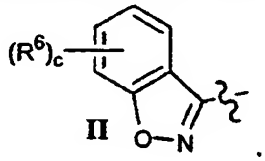
(A) aryl;

(B) substituted aryl, wherein the substituents on said substitued aryl are selected from: (1) halo; or (2) alkyl; or (3) substituted alkyl;

(C) heteroaryl;

(D) substituted heteroaryl; or

(E) when R^1 is taken together with X, then the moiety is



3. (currently amended) The ~~compound~~ composition of Claim 2 wherein R^1 is selected from:

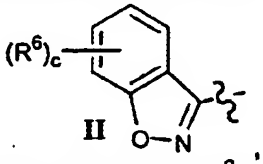
(A) phenyl;

(B) substituted phenyl wherein the substituents on said substitued phenyl are selected from: (1) halo; (2) alkyl; (3) alkyl substituted with halo;

(C) heteroaryl selected from: pyridyl, thienyl, pyrimidinyl, thiazolyl or pyridyl N-Oxide;

(D) alkyl substituted thiazolyl; or

(E) when R^1 is taken together with X, then the moiety is



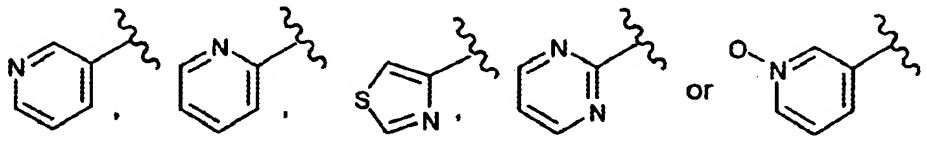
wherein c is 0 or 1, and when c is 1 then R^6 is halo.

4. (currently amended) The ~~compound~~ composition of Claim 3 wherein R^1 is selected from:

(A) phenyl;

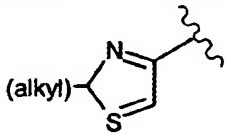
(B) substituted phenyl, wherein the substituents on said substitued phenyl are independently selected from: chloro, fluoro or trifluoromethyl;

(C) heteroaryl selected from:



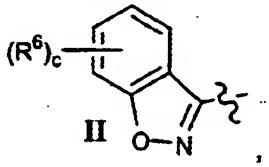
or

(D) substituted heteroaryl of the formula:



; or

(E) when R^1 is taken together with X, then the moiety is



wherein c is 0 or 1, and when c is 1 then R^6 is fluoro.

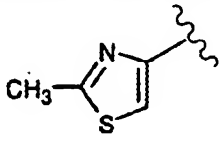
5. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein R^1 is selected from:

(A) phenyl;

(B) substituted phenyl, wherein the substituents on said substitued phenyl are independently selected from: chloro, fluoro or trifluoromethyl;

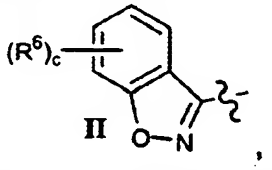
(C) pyridyl; or

(D) substituted heteroaryl of the formula:



; or

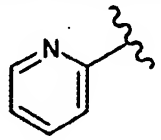
(E) when R^1 is taken together with X, then the moiety is



wherein c is 0 or 1, and when c is 1 then R^6 is fluoro.

6. (currently amended) The ~~compound~~ composition of Claim 5 wherein R^1 is pyridyl.

7. (currently amended) The ~~compound~~ composition of Claim 6 wherein R^1 is



8. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein X is $=C(NOR^3)$, and R^3 is selected from H or alkyl.

9. (currently amended) The ~~compound~~ composition of Claim 8 wherein R^3 is selected from H, methyl or ethyl.

10. (currently amended) The ~~compound~~ composition of Claim 9 wherein R^3 is methyl.

11. (currently amended) The ~~compound~~ composition of claim [[1]] 56 wherein: (1) M^2 is nitrogen; and (2) M^3 and M^4 are selected such that: (a) one is carbon and the other is nitrogen, or (b) both are nitrogen.

12. (currently amended) The ~~compound~~ composition of Claim 11 wherein M^3 is carbon, and M^4 is nitrogen.

13. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein:

n is 2;.

a is 0 or 1;

b is 0 or 1;

c is 0 or 1, and when c is 1 then R^6 is halo;

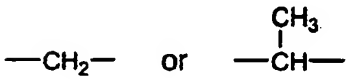
e is 1 to 5; and

p is 2.

14. (currently amended) The ~~compound~~ composition of claim [[1]] 56 wherein Y is =C(O).

15. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein Z is C_1 to C_3 alkyl.

16. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein Z is

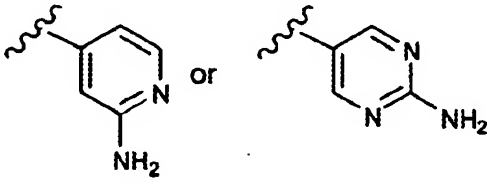


17. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein R^2 is a six membered heteroaryl ring.

18. (currently amended) The ~~compound~~ composition of Claim 17 wherein R^2 is selected from pyridyl, pyridyl substituted with $-NR^4R^5$, pyrimidinyl, or pyrimidinyl substituted with $-NR^4R^5$.

19. (currently amended) The ~~compound~~ composition of Claim 18 wherein R^2 is pyridyl substituted with $-NH_2$, or pyrimidinyl substituted with $-NH_2$.

20. (currently amended) The ~~compound~~ composition of Claim 19 wherein R^2 is



21. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein R^4 is H or lower alkyl; R^5 is H, C_1 to C_6alkyl, or $-C(O)R^4$; R^{12} is alkyl, hydroxy or fluoro; and R^{13} is alkyl, hydroxy or fluoro.

22. (currently amended) The ~~compound~~ composition of Claim 21 wherein R^4 is H or methyl; R^5 is H or methyl; R^{12} is hydroxy or fluoro; and R^{13} is hydroxy or fluoro.

23. (currently amended) The ~~compound~~ composition of Claim [[1]] 56 wherein:

(1) R^1 is selected from:

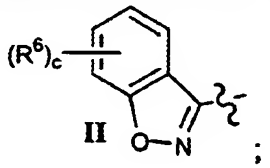
(A) aryl;

(B) substituted aryl, wherein the substituents on said substitued aryl are selected from: (1) halo; or (2) alkyl; or (3) substituted alkyl;

(C) heteroaryl; or

(D) substituted heteroaryl; or

(E) when R^1 is taken together with X, then the moiety is



;

(2) X is $=C(NOR^3)$;

(3) R^3 is selected from H or alkyl;

(4) M^2 is nitrogen;

(5) Y is =C(O);

(6) M^3 and M^4 are selected such that: (1) one is carbon and the other is nitrogen, or (2) both are nitrogen;

(7) Z is C_1 to C_3 alkyl; and

(8) R^2 is a six membered heteroaryl ring.

24. (currently amended) The ~~compound~~ composition of Claim 23 wherein:

(1) R^1 is selected from:

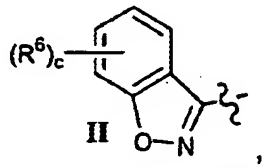
(A) phenyl;

(B) substituted phenyl wherein the substituents on said substitued phenyl are selected from: (1) halo; (2) alkyl; (3) alkyl substituted with halo;

(C) heteroaryl selected from: pyridyl, thienyl, pyrimidinyl, thiazolyl or pyridyl N-Oxide; or

(D) alkyl substituted thiazolyl; or

(E) when R^1 is taken together with X, then the moiety is



wherein c is 0 or 1, and when c is 1 then R^6 is halo;

(2) R^3 is selected from H, methyl or ethyl;

(3) n is 2,

(4) a is 0 or 1,

(5) b is 0 or 1,

(6) c is 0 or 1 and when c is 1 then R^6 is halo,

(7) e is 1 to 5,

(8) p is 2,

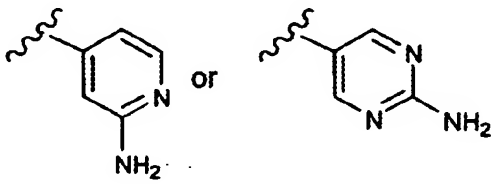
(9) R^4 is H or lower alkyl,

(10) R^5 is H, C_1 to C_6alkyl, or $-C(O)R^4$;

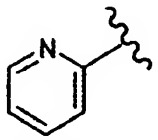
(11) R^{12} is alkyl, hydroxy or fluoro, and

(12) R^{13} is alkyl, hydroxy or fluoro.

25. (currently amended) The ~~compound~~ composition of Claim 24 wherein R^2 is



R^1 is



M^2 is nitrogen, M^3 is carbon, and M^4 is nitrogen.

26 to 43. (cancelled)

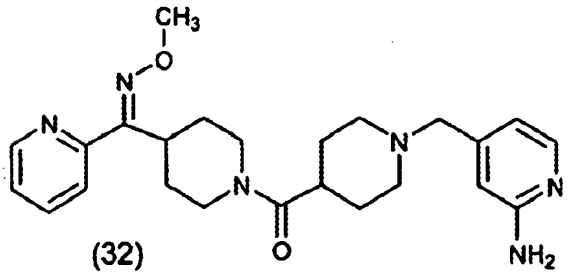
44. (currently amended) The method of Claim [[43]] 57 wherein said H_1 receptor antagonist is selected from: astemizole, azatadine, azelastine, acrivastine, brompheniramine, cetirizine, chlorpheniramine, clemastine, cyclizine, carebastine, cyproheptadine, carbinoxamine, descarboethoxyloratadine, diphenhydramine, doxylamine, dimethindene, ebastine, epinastine, efletirizine, fexofenadine, hydroxyzine, ketotifen, loratadine, levocabastine, meclizine, mizolastine, mequitazine, mianserin, noberastine, norastemizole, picumast, pyrilamine, promethazine, terfenadine, tripelennamine, temelastine, trimeprazine or triprolidine.

45. (original) The method of Claim 44 wherein said H_1 receptor antagonist is selected from: loratadine, descarboethoxyloratadine, fexofenadine or cetirizine.

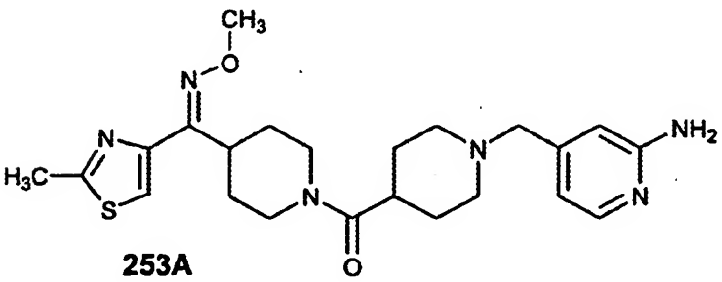
46. (original) The method of Claim 45 wherein said H_1 receptor antagonist is selected from: loratadine or descarboethoxyloratadine.

47 to 50. (cancelled)

51. (currently amended) A pharmaceutical composition ~~comprising an effective amount of a compound of Claim 1~~ of Claim 56, ~~and an effective amount of H_1 receptor antagonist, and a pharmaceutically effective carrier,~~ wherein said compound of ~~Claim 1~~ formula I is selected from:



(32) ;



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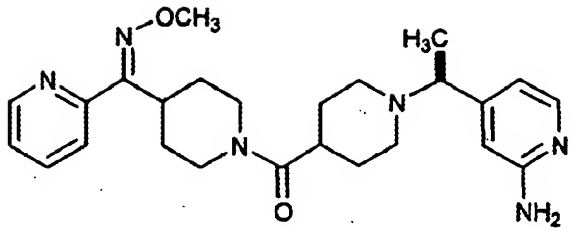
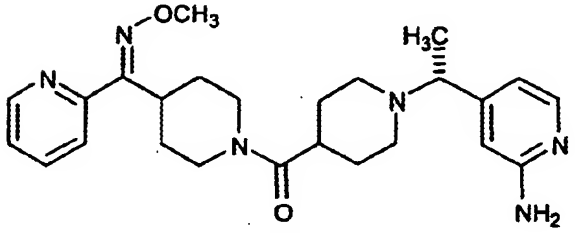


54 ;



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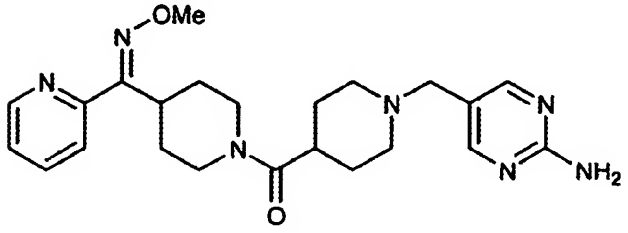
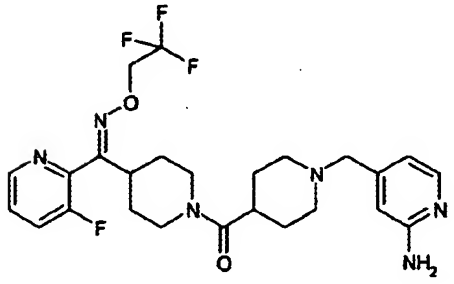
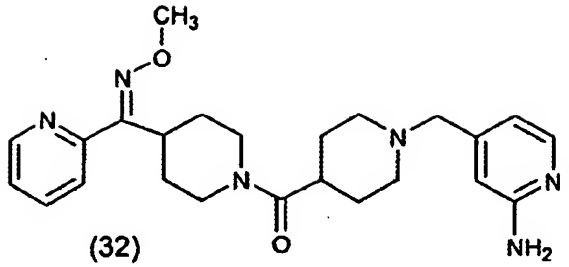


287 ; or



52. (currently amended) A method of ~~treating: allergy, allergy-induced airway responses, and congestion comprising administering to a patient in need of such treatment an effective amount of a compound of Claim 1 in combination with an effective amount of an H_1 receptor antagonist,~~ Claim 57 wherein said compound of ~~Claim 1~~ formula I is selected from:



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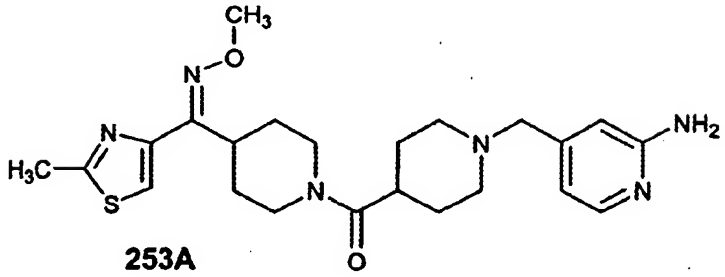

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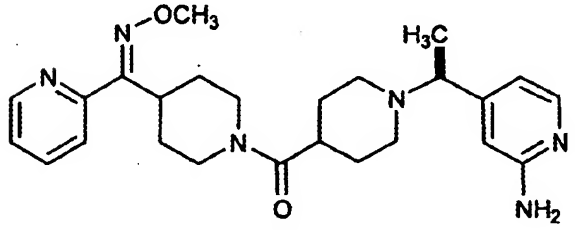
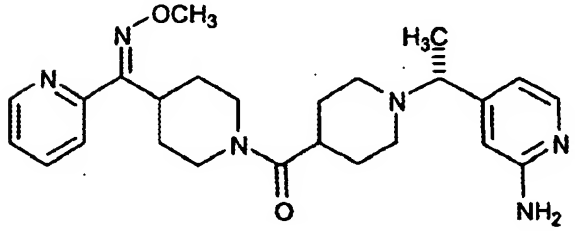


54 ;



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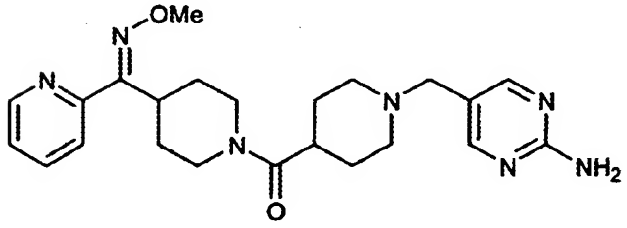
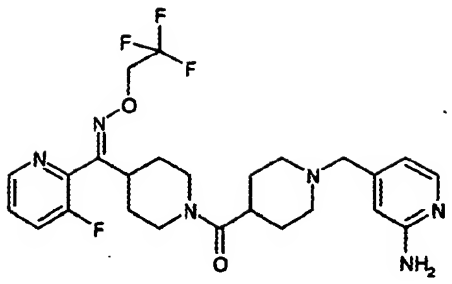


287 ; or

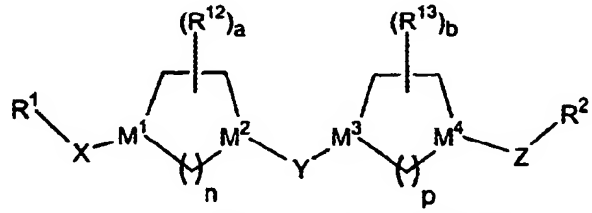


53. (original) The method of Claim 52 wherein said H_1 receptor antagonist is selected from: astemizole, azatadine, azelastine, acrivastine, brompheniramine, cetirizine, chlorpheniramine, clemastine, cyclizine, carebastine, cyproheptadine, carbinoxamine, descarboethoxyloratadine, diphenhydramine, doxylamine, dimethindene, ebastine, epinastine, efletirizine, fexofenadine, hydroxyzine, ketotifen, loratadine, levocabastine, meclizine, mizolastine, mequitazine, mianserin, noberastine, norastemizole, picumast, pyrilamine, promethazine, terfenadine, tripelennamine, temelastine, trimeprazine or triprolidine.

54. (original) The method of Claim 53 wherein said H_1 receptor antagonist is selected from: loratadine, descarboethoxyloratadine, fexofenadine or cetirizine.

55. (original) The method of Claim 54 wherein said H_1 receptor antagonist is selected from: loratadine or descarboethoxyloratadine.

56. (new) A pharmaceutical composition comprising an effective amount of a compound of the formula I:



(I)

or a pharmaceutically acceptable salt or solvate thereof, wherein:

(1) R^1 is is selected from:

(a) aryl;

(b) heteroaryl;

(c) heterocycloalkyl

(d) alkyl;

(e) cycloalkyl; or

(f) alkylaryl;

wherein said R^1 groups are optionally substituted with 1 to 4 substituents independently selected from:

(1) halogen;

(2) hydroxyl;

(3) lower alkoxy;

(4) $-CF_3$;

(5) CF_3O-;

(6) $-NR^4R^5$;

(7) phenyl;

(8) $-NO_2$,

(9) $-CO_2R^4$;

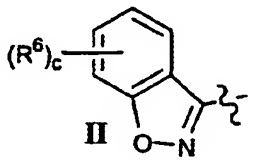
(10) $-CON(R^4)_2$ wherein each R^4 is the same or different;

(11) $-S(O)_mN(R^{20})_2$ wherein each R^{20} is the same or different H or alkyl group;

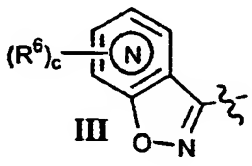
(12) -CN; or

(13) alkyl; or

(2) R^1 and X taken together form a group selected from:

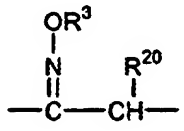


or



wherein (N) represents a nitrogen atom located at one of the 4 non-fused positions of the ring;

(3) X is selected from: =C(O), $=C(NOR^3)$, $=C(NNR^4R^5)$,



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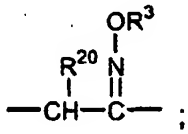


;

(4) M^1 is carbon;

(5) M^2 is selected from C or N;

(6) M^3 and M^4 are independently selected from C or N;

(7) Y is selected from: is $-CH_2-$, $=C(O)$, $=C(NOR^{20})$ (wherein R^{20} is as defined above), or $=C(S)$;

(8) Z is a $C_1 - C_6$ alkyl group;

(9) R^2 is a five or six-membered heteroaryl ring, said six-membered heteroaryl ring comprising 1 or 2 nitrogen atoms with the remaining ring atoms being carbon, and said five-membered heteroaryl ring containing 1 or 2 heteroatoms selected from: nitrogen, oxygen, or sulfur with the remaining ring atoms being carbon; said five or six membered heteroaryl rings being optionally substituted with 1 to 3 substituents independently selected from: halogen, hydroxyl, lower alkyl, lower alkoxy, $-CF_3$, CF_3O-, $-NR^4R^5$, phenyl, $-NO_2$, $-CO_2R^4$, $-CON(R^4)_2$ wherein each R^4 is the same or different, $-CH_2NR^4R^5$, $-(N)C(NR^4R^5)_2$, or -CN;

(10) R^3 is selected from:

(a) hydrogen;

(b) $C_1 - C_6$ alkyl;

(c) aryl;

(d) heteroaryl;

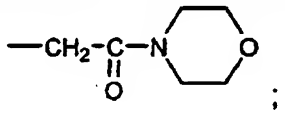
(e) heterocycloalkyl;

(f) arylalkyl;

(g) $-(CH_2)_e-C(O)N(R^4)_2$ wherein each R^4 is the same or different,

(h) $-(CH_2)_e-C(O)OR^4$;

(i) $-(CH_2)_e-C(O)R^{30}$ wherein R^{30} is a heterocycloalkyl group, or



;

(j) $-CF_3$; or

(k) $-CH_2CF_3$;

wherein said aryl, heteroaryl, heterocycloalkyl, and the aryl portion of said arylalkyl are optionally substituted with 1 to 3 substituents selected from: halogen, -OH, $-OCF_3$, $-CF_3$, -CN, $-N(R^{45})_2$, $-CO_2R^{45}$, or $-C(O)N(R^{45})_2$, wherein each R^{45} is independently selected from: H, alkyl, alkylaryl, or alkylaryl wherein said aryl moiety is substituted with 1 to 3 substituents independently selected from $-CF_3$, -OH, halogen, alkyl, $-NO_2$, or -CN;

(11) R^4 is selected from: hydrogen, $C_1 - C_6$ alkyl, aryl, alkylaryl, said aryl and alkylaryl groups being optionally substituted with 1 to 3 substituents selected from: halogen, $-CF_3$, $-OCF_3$, -OH, $-N(R^{45})_2$, $-CO_2R^{45}$, $-C(O)N(R^{45})_2$, or –CN; wherein R^{45} is as defined above;

(12) R^5 is selected from: hydrogen, $C_1 - C_6$ alkyl, $-C(O)R^4$, $-C(O)_2R^4$, or $-C(O)N(R^4)_2$ wherein each R^4 is independently selected, and R^4 is as defined above;

(13) or R^4 and R^5 taken together with the nitrogen atom to which they are bound forms a five or six membered heterocycloalkyl ring;

(14) R^6 is selected from: alkyl, aryl, alkylaryl, halogen, hydroxyl, lower alkoxy, $-CF_3$, CF_3O-, $-NR^4R^5$, $-NO_2$, $-CO_2R^4$, $-CON(R^4)_2$ wherein each R^4 is the same or different, or -CN;

(15) R^{12} is selected from: alkyl, hydroxyl, alkoxy, or fluoro;

(16) R^{13} is selected from: alkyl, hydroxyl, alkoxy, or fluoro;

(17) a is 0 to 2;

(18) b is 0 to 2;

(19) c is 0 to 2;

(20) e is 0 to 5;

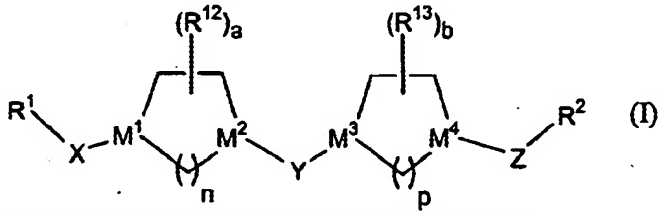
(21) m is 1 or 2;

(22) n is 1, 2 or 3; and

(23) p is 1, 2 or 3, with the proviso that when M^3 and M^4 are both nitrogen, then p is 2 or 3;

and an effective amount of H_1 receptor antagonist, and a pharmaceutically effective carrier.

57. (new) A method of treating: allergy, allergy-induced airway responses, and congestion comprising administering to a patient in need of such treatment an effective amount of a compound of formula I:



(I)

or a pharmaceutically acceptable salt or solvate thereof, wherein:

(1) R^1 is is selected from:

(a) aryl;

(b) heteroaryl;

(c) heterocycloalkyl

(d) alkyl;

(e) cycloalkyl; or

(f) alkylaryl;

wherein said R^1 groups are optionally substituted with 1 to 4 substituents independently selected from:

(1) halogen;

(2) hydroxyl;

(3) lower alkoxy;

(4) $-CF_3$;

(5) CF_3O-;

(6) $-NR^4R^5$;

(7) phenyl;

(8) $-NO_2$,

(9) $-CO_2R^4$;

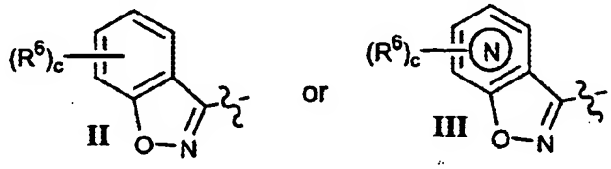
(10) $-CON(R^4)_2$ wherein each R^4 is the same or different;

(11) $-S(O)_mN(R^{20})_2$ wherein each R^{20} is the same or different H or alkyl group;

(12) -CN; or

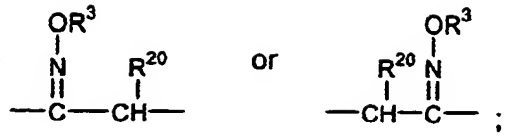
(13) alkyl; or

(2) R^1 and X taken together form a group selected from:



wherein (N) represents a nitrogen atom located at one of the 4 non-fused positions of the ring;

(3) X is selected from: =C(O), $=C(NOR^3)$, $=C(NNR^4R^5)$,



(4) M^1 is carbon;

(5) M^2 is selected from C or N;

(6) M^3 and M^4 are independently selected from C or N;

(7) Y is selected from: is $-CH_2-$, =C(O), $=C(NOR^{20})$ (wherein R^{20} is as defined above), or =C(S);

(8) Z is a $C_1 - C_6$ alkyl group;

(9) R^2 is a five or six-membered heteroaryl ring, said six-membered heteroaryl ring comprising 1 or 2 nitrogen atoms with the remaining ring atoms being carbon, and said five-membered heteroaryl ring containing 1 or 2 heteroatoms selected from: nitrogen, oxygen, or sulfur with the remaining ring atoms being carbon; said five or six membered heteroaryl rings being optionally substituted with 1 to 3 substituents independently selected from: halogen, hydroxyl, lower alkyl, lower alkoxy, $-CF_3$, CF_3O-, $-NR^4R^5$, phenyl, $-NO_2$, $-CO_2R^4$, $-CON(R^4)_2$ wherein each R^4 is the same or different, $-CH_2NR^4R^5$, $-(N)C(NR^4R^5)_2$, or -CN;

(10) R^3 is selected from:

(a) hydrogen;

(b) $C_1 - C_6$ alkyl;

(c) aryl;

(d) heteroaryl;

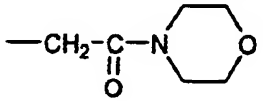
(e) heterocycloalkyl;

(f) arylalkyl;

(g) $-(CH_2)_e-C(O)N(R^4)_2$ wherein each R^4 is the same or different,

(h) $-(CH_2)_e-C(O)OR^4$;

(i) $-(CH_2)_e-C(O)R^{30}$ wherein R^{30} is a heterocycloalkyl group, or



(j) $-CF_3$; or

(k) $-CH_2CF_3$;

wherein said aryl, heteroaryl, heterocycloalkyl, and the aryl portion of said arylalkyl are optionally substituted with 1 to 3 substituents selected from:

halogen, -OH, -OCF_3, -CF_3, -CN, -$N(R^{45})_2$, -CO_2R^{45}, or -$C(O)N(R^{45})_2$, wherein each R^{45} is independently selected from: H, alkyl, alkylaryl, or alkylaryl wherein said aryl moiety is substituted with 1 to 3 substituents independently selected from –CF_3, -OH, halogen, alkyl, -NO_2, or -CN;

(11) R^4 is selected from: hydrogen, $C_1 - C_6$ alkyl, aryl, alkylaryl, said aryl and alkylaryl groups being optionally substituted with 1 to 3 substituents selected from: halogen, -CF_3, -OCF_3, -OH, -$N(R^{45})_2$, -CO_2R^{45}, -$C(O)N(R^{45})_2$, or –CN; wherein R^{45} is as defined above;

(12) R^5 is selected from: hydrogen, $C_1 - C_6$ alkyl, -$C(O)R^4$, -$C(O)_2R^4$, or -$C(O)N(R^4)_2$ wherein each R^4 is independently selected, and R^4 is as defined above;

(13) or R^4 and R^5 taken together with the nitrogen atom to which they are bound forms a five or six membered heterocycloalkyl ring;

(14) R^6 is selected from: alkyl, aryl, alkylaryl, halogen, hydroxyl, lower alkoxy, -CF_3, CF_3O-, -NR^4R^5, -NO_2, -CO_2R^4, -$CON(R^4)_2$ wherein each R^4 is the same or different, or -CN;

(15) R^{12} is selected from: alkyl, hydroxyl, alkoxy, or fluoro;

(16) R^{13} is selected from: alkyl, hydroxyl, alkoxy, or fluoro;

(17) a is 0 to 2;

(18) b is 0 to 2;

(19) c is 0 to 2;

(20) e is 0 to 5;

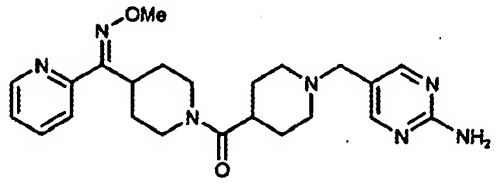
(21) m is 1 or 2;

(22) n is 1, 2 or 3; and

(23) p is 1, 2 or 3, with the proviso that when M^3 and M^4 are both nitrogen, then p is 2 or 3;

in combination with an effective amount of an H_1 receptor antagonist.

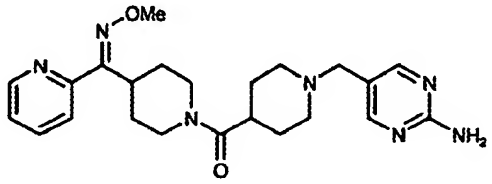
58. (new) A pharmaceutical composition comprising an effective amount of a compound of the formula



and an effective amount of H_1 receptor antagonist, and a pharmaceutically effective carrier.

59. (new) The composition of claim 58 wherein the H_1 receptor antagonist is selected from loratadine or descarboethoxyloratadine.

60. (new) A method of treating: allergy, allergy-induced airway responses, and congestion comprising administering to a patient in need of such treatment an effective amount of a compound of the formula



in combination with an effective amount of an H_1 receptor antagonist.

61. (new) The method of claim 60 wherein the H_1 receptor antagonist is selected from loratadine or descarboethoxyloratadine.